Lean tenometer. The irides were violently inflamed; the anterior chambers were full of floating cells and a fibrinous exudate. A deep keratitis began at one side of the right cornea and had gradually extended into part of the pupillary area. The vision in both eyes was limited to the perception of hand movements at a distance of a few feet. The general physical examination, the urine and blood Wassermann were negative. The blood count was not remarkable.

The youth of the patient, the presence of the recent violent inflammatory reaction in the immediate neighborhood of the eyes, and close contact with an extensive case of impetigo in the same family, made me very hesitant to undertake any operative procedure.

One dose of suprarenin bitartrate was administered to both eyes. This resulted in the elevation of the intraocular tension in both eyes and a fairly wide dilatation of both pupils, and in greatly increasing the discomfort and apprehension of the patient. The day after the administration of the suprarenin bitartrate, Doctor Josephson's reprint arrived. I found that the substance was available under the name of Eschatin (Parke, Davis & Company); and after a consultation with Dr. Chauncey Leake, professor of pharmacology at the University of California, and Dr. Garnet Cheney, who had used the substance extensively in the treatment of Addison's disease, I decided to use it intravenously. One cubic centimeter was administered intravenously on August 28, 1935. Immediately before administration the tension was 60 in the right eye and 55 in the left by the McLean tenometer. Before the needle was withdrawn from the vein, the patient sat up and remarked that she saw better. I ascribed this to the Italian temperament; but in thirty-five minutes I again took the tension with the tenometer and could hardly believe my eyes when both eyes registered 45, McLean. The substance has been administered intravenously in doses of 1 cubic centimeter daily since, each time with a marked drop in the tension and a corresponding improvement in vision.

As soon as it was considered safe, her hypertrophied, infected tonsils were removed, and she has since shown slow but steady improvement. The cortin has tided her over the acute stage and saved her eyes from surgical operation, which at best is not very satisfactory in this type of case.

This experience leads me to believe that cortin has a very definite place in the treatment of glaucoma. It is, of course, probable that the more frequent administration would be advantageous. It would be interesting to investigate the possibility that the occasional beneficial effect of epinephrin in glaucoma may be due to an admixture of cortin, and to determine if instillation in the conjunctival sac is effective.

490 Post Street.

GEORGE N. HOSFORD,
San Francisco.

NARCOSIS AND OXIDATIVE MECHANISMS OF THE BRAIN

In 1930 V. E. Henderson suggested, in *Physiological Reviews,* that the evidence then at hand was inadequate to support any theory linking narcosis with inhibition of normal oxidative processes in the brain. Despite the abundant and painstaking subsequent biochemical work by Holmes, Bülow, Ashford, Dixon, Peters, Rydin, Quastel and Wheatley, and others in England, and Wortis, Fenn, Gross and Pierce and others in this country, the ultimate solution of this pharmacologic problem has not been greatly clarified.

The case for a direct relation of narcosis and brain oxidations is based on this triad: (*a*) *certain* narcotic agents, as the barbiturates,[1] act on isolated surviving brain tissue to inhibit the oxidative enzyme system dealing with glucose, lactic and pyruvic acids in about the same concentration as is presumably present in very deep narcosis; also, after deep chloroform anesthesia,[1] but not morphin narcosis,[2] the surviving brain from animals so treated shows a perceptible decrease of respiration; (*b*) in a homologous series of narcotics, again taking the barbiturates as the best example, the degree of inhibition of oxygen consumption of surviving brain varies directly with the narcotic potency; and (*c*) the success of treating chronic depressive states in the insane by means of long-continued narcosis.

Failure to explain other experimental findings, however, detracts seriously from the acceptability of any theory relating brain oxidative rates and narcosis. These may be summarized as: (*a*) concentrations of drugs active on the carbohydrate oxidation system *in vitro* are in many cases far beyond those producing narcosis in the intact animal; (*b*) satisfactory evidence of segregation of drug in the brain *in vivo,*[3] or of enhanced susceptibility of anatomically discrete centers to inhibition of glucose metabolism has been lacking, although it is imperative that such a condition exist if the lack of activity of narcotics on whole minced-brain tissue is to be reconciled with their narcotic activity through depressing oxygen consumption; (*c*) active agents of types other than narcotics produce reversible changes in the oxidative rate of surviving brain tissue closely resembling[4] those brought about by narcotics even though of the amins so acting,[4] phenylethylamin and others may function in the lightly narcotized intact animal as cerebral excitants; (*d*) observations made on inhibitions of extra uptake of oxygen by treated autoxidized brain to which glucose is added may pertinently be objected to, since the oxidative processes in brain tissue have been shown through use of the catatorulin[5] effect

1 Quastel, J. H., and Wheatley, A. H. M.: Proc. Royal Soc., B, 112, 1932.

2 Gross, E. G., and Pierce, I. H.: Jour. Pharmacol. Exper. Therap., 53,156, 1935.

3 Koppanyi, T., and Dille, J. M.: Jour. Pharmacol. Exper. Therap., 54:84, 1935.

4 Quastel, J. H., and Wheatley, A. H. M.: Biochem. J., 27:1609, 1933; 28:1521, 1934.

5 Peters, R. A., Rydin, H., and Thompson, R. H. S.: Biochem. J., 29:53, 1935.

to be mediated by chain reactions; (*e*) passive or narcotized nervous tissue consumes considerable oxygen simply to maintain itself, and the increase during activity is slight as compared to muscular tissue; (*f*) it is questionable whether the same mechanisms of oxidation function in surviving brain as in the intact animal;[6] and (*g*) the study of tissue *in vitro* yields a partial picture only, in any case, since general humoral effects are absent.

Thus, while isolated tissue work on surviving brain is yielding much sound biochemical information, as to oxidative mechanisms present, the effects of agents such as potassium, phosphate, or vitamin B, and the availability of different substrates, the difficulties of obtaining significant pharmacologic data are such that perhaps little real progress can be made for some time. Meanwhile, such studies as those of Meyer and his coworker[7] point out interesting relationships between physical properties of agents and their narcotic potency, suggesting an explanation of narcosis which may be less mysterious than the postulated selective inhibitory action of narcotics on the lactic dehydrogenase of certain ill-defined centers.

Pharmacological Laboratory,
University of California.

C. D. LEAKE, Ph. D.,
G. A. EMERSON, Ph. D.,
San Francisco.

AUTOCYTOTOXIC "ANTIBODIES?"

Among the speculative immunologic theories of current interest, none is of wider clinical application than the tentative hypothesis that certain progressive degenerative diseases of highly specialized parenchymatous tissues are due to an auto-immunologic, or auto-allergic vicious circle. This theory assumes that, as a result of an initial toxic or infectious injury, certain highly specialized organ-specific tissues colloids are so denatured as to render them specifically antigenic for their animal of origin. The resultant antiorgan-specific immunity may conceivably be due to "antibodies" specifically cytotoxic for normal homologous tissues. These autocytotoxins may conceivably be formed in sufficient amounts to cause perversion or suppression of homologous tissue function, with ultimate atrophy or degeneration.

This futuristic theory is an apparently logical deduction from the rapidly increasing number of organ-specific proteins, lipoids, and carbohydrates now recognized in animal tissues. Some of these specific organic products are known to require but slight chemical or physicochemical alteration to render them specifically antigenic for the same animal species.

Hektoen and Schulhof,[1] for example, found that the organ-specific proteins of the crystalline lens of the rabbit eye are not demonstrably antigenic for rabbits, causing the production of no demonstrable antilens precipitins. Burkey, Woods, and Woodhall,[2] however, found that normal rabbit lens proteins can be separated into three crystalline factors, one of which is highly antigenic for rabbits, if freed from the "inhibiting" action of the other two factors. The "fractional antibodies" thus formed may presumably reach a sufficiently high titer in actively immunized rabbits to cause autocytotoxic cataract.

One would suspect from this finding that certain local bacterial infections might so denature the organ-specific factors in the liver, kidney, thyroid gland, and central nervous system, for example, as to set up a similar immunochemical vicious circle, leading to progressive degenerative lesions of these organs. The latest apparent confirmations of this fear are the production, by Doctors Rivers and Schwenther[3] of the Rockefeller Institute, of progressive degenerative lesions of the central nervous system as a result of heterophile antibrain immunization.

Doctors Rivers and Schwenther gave eight monkeys repeated intramuscular injections with normal rabbit brain emulsions alternated with normal rabbit brain lipoids. Brain lipoids are known to be organic-specific haptenes, which are rendered auto-antigenic by adsorption on an appropriate colloidal "carrier." After forty or more injections with these heterophile brain antigens, seven of Doctor Rivers' actively immunized monkeys began to show signs of ataxia. The ataxia became progressively worse and in certain cases ended in definite paralysis. Histologic study showed marked degenerative lesions of these ataxic or paralytic monkey brains, accompanied by extensive local demyelinization.

The New York investigators, however, very carefully avoid a definite conclusion as to the probable immunochemical mechanism involved in this experimental encephalomyelitis. They did rule out, however, the possibility that the encephalomyelitis is due to an intercurrent infection. No bacteria were demonstrable in the degenerated brains, nor were they demonstrably infectious on intracerebral injections into normal monkeys, rabbits, guinea-pigs, or mice. The possibility that the encephalomyelitis might be due to an environmental virus, nonpathogenic for normal animals, but pathogenic for animals subjected to the repeated toxic injury incident to heterophile immunization, has not yet been tested.

Box 51, Stanford University.

W. H. MANWARING,
Stanford University.

6 Ashford, C. A., and Dixon, K. C.: Biochem. J., 29:167, 1935.

7 Meyer, K. H., and Hemmi, H.: Biochem. Z., 277:39, 1935.

1 Hektoen, L., and Schulhof, K.: J. Infect. Dis., 34:433, 1924.

2 Burkey, E. L., Woods, A. C., and Woodhall, M. B.: Arch. Ophth., 9:446, 1933.

3 Rivers, T. M., and Schwenther, F. F.: J. Exper. Med., 61:689 (May), 1935.

Sickness is very wasteful of time and money, as well as a disagreeable and alarming experience. It cuts off income and increases expenses. It threatens all that we hold most worth while—our ambitions, careers, usefulness to the community; our homes, friends, and families. It is the greatest obstacle to a serene, happy, contented, useful life. — Franklin D. Roosevelt.